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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/939,483	08/24/2001	Fabrice Duprat	1201-CIP-DIV-2-00	3851

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EXAMINER

BERTOGLIO, VALARIE E

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 11/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/939,483	DUPRAT ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 September 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 29-33 is/are pending in the application.
- 4a) Of the above claim(s) 29-31 and 33 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 32 is/are rejected.
- 7) ☒ Claim(s) 32 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 August 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group II, claim 32 in the response received 09/08/2003 is acknowledged. Claims 1-28 have been cancelled. Claims 29-31 and 33 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse. Claim 32 is under current examination.

Specification

The disclosure is objected to because of the following informalities: In the Description of the Figures (page 4-8), Figure descriptions should contain a heading for each figure described in a paragraph. For example, page 4, line 13 should begin "Figures 1A-1C"; page 4, line 23 should begin "Figures 2A-2B"; page 5, line 7 should begin "Figures 3A-3F"; page 5, line 4 should begin "Figures 4A-4C"; page 5, line 24 should begin "Figures 5A-5D"; page 6, line 6 should begin "Figures 6A-6G"; page 6, line 20 should begin "Figures 7A-7D"; page 7, line 5 should begin "Figures 8A-8B"; page 7, line 12 should begin "Figures 9A-9B"; page 7, line 24 should begin "Figures 11A-11D"; page 8, line 8 should begin "Figures 12A-12F"; page 9, line 15 should begin "Figures 13A-13D".

Appropriate correction is required.

Claim Objections

Claim 32 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the

claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 32 is drawn to a transgenic knockout animal lacking expression of the potassium transport channel encoded by the nucleic acid sequence represented by SEQ ID NO:3. Claim 32 depends from claim 29, which is drawn to a transgenic animal comprising a transgene encoding a potassium transport channel. The claims encompass animals that are mutually exclusive and therefore, claim 32 cannot further limit claim 29.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The claimed invention is directed to non-statutory subject matter. Claim 32, as written, encompasses a transgenic human, which is non-statutory subject matter. Changing claim 32 to read transgenic non-human animal would obviate this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 32 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 32 is directed to a transgenic animal that is deficient for the expression of the potassium transport channel encoded by the nucleic acid sequence set forth in SEQ ID NO:3. Claim 32 depends from claim 29, which is directed to a transgenic animal comprising a transgene encoding a potassium channel. Because a transgenic animal cannot comprise a transgene and be deficient for it simultaneously, claim 32 is being interpreted as it relates to the elected invention of a transgenic knockout animal deficient for a potassium transport channel (refer to Election/Restriction, mailed 07/16/2003, page 2, Group II).

1) The specification fails enable any species of knockout animal other than mouse. The breadth of the claims is such that they encompass any species of animal. The art at the time of filing held that targeted gene insertion technology was not available for any species other than mouse. Since homologous recombination is required for gene targeting methods, embryonic stem cell technology must be available to carry out the method. Campbell and Wilmut (1997, *Theriogenology*, vol. 47, pp. 63-72) acknowledge reports of ES-like cells in a number of species, but emphasize that as yet there are no reports of any cell lines that contribute to the germ line in any species other than mouse (page 65). Zan (2003, *Nature Biotech*, Vol. 21, pages 645-651) taught that the knockout technology that is key to using the mouse as a genetic model is not even available for the closely related rat and proposes an alternative genetic strategy for rats that does not require totipotent ES cells. Potential methods of generating transgenic embryos in other non-mouse species using homologous recombination had not been developed at the time the invention was made (McGreath, 2000, *Nature*, Vol. 405, pages 1066-1069; Kent-First, 2000, *Nature Biotechnology*, Vol. 18, pages 928-929; Dinnyes, 2002, *Cloning and Stem Cells*, Vol. 4,

pages 81-90). Thus, at the time of filing, knockout animals could not be prepared for any species other than mouse.

The specification teaches the cloning and characterization of TASK, a TWIK-related K⁺ channel (pages 16-23). The specification contemplates generating transgenic animals that either supra-express a protein of the TASK family of potassium channels or a knock-out animal deficiency for said channels (page 28, lines 12-18). While it is well known in the art how to generate a knockout mouse lacking a particular gene product, the specification does not provide any guidance as to how to overcome failure of ES cells in non-mouse species to populate the germline in generating non-mouse knockout animals. It would require undue experimentation for one of skill in the art at the time of filing to determine how to generate a knockout animal of any species other than mouse.

2) The transgenic animals of claim 32 do not have a phenotype and the claim encompasses a transgenic animal having any phenotype. The specification fails to enable one of skill in the art to determine the phenotype of the mouse claimed or how to use the mouse.

The art at the time of filing held that the phenotype of transgenic animals was unpredictable. Leonard (1995, Immunological Reviews, Vol. 148, pages 98-113) disclosed mice with a disruption in the *g_c* gene that was intended to be a model for X-linked severe combined immunodeficiency (XSCID), but display a variety of unexpected traits (abstract). These knockout mice were expected to have thymocytes with decreased proliferation in response to stimulation with antibodies, but the thymocytes proliferated normally (page 105, line 7). Griffiths (1998, Microscopy Research and Technique, Vol. 41, pages 344-358) taught that,

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despite a known role for the PLP gene based on spontaneous mutations in the gene, the knockout mouse failed to display any of the expected phenotypes (page 350, last paragraph).

The specification contemplates generating a knock-out animal deficient for potassium transport channels (page 28, lines 12-18); however, the specification fails to teach how to generate such an animal that has any phenotype. Because the phenotype of a knockout is unpredictable, one cannot guess what the phenotype of the claimed animal might be and one cannot determine, a priori, how to generate the claimed animal such that it has any particular phenotype.

Furthermore, without a recitation of a phenotype in the claim, one would not know when they had attained the claimed animal. One of skill in the art would not know how to use the claimed animal that has any phenotype. Therefore, it would require one of skill in the art at the time the invention was made, undue experimentation to determine how to generate the claimed animal such that it has any phenotype and how to use said animal having any phenotype.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 32 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 32 is unclear as it is drawn to a knockout animal which is deficient for expression of the potassium transport channel encoded by the nucleic acid sequence represented by SEQ ID NO:3, however, depends from claim 29 which is drawn to a transgenic animal expressing a transgene encoding a potassium transport channel. It is unclear if the claim, as written, is

referring to an animal comprising a transgene comprising a potassium transport channel other than that encoded by SEQ ID NO:3 and is deficient for expression of SEQ ID NO:3 or is referring to some other animal.

Claim 32 is further unclear due to the use of the term “represented” in line 3. It is not clear what the nucleic acid sequence set forth by SEQ ID NO: 3 is meant to represent.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 32 is rejected under 35 U.S.C. 102(b) as being anticipated by Mullins (1990, Nature, Vol. 344, pages 541-544).

Claim 32 is drawn to a transgenic animal of any species that is deficient for expression of the potassium transport channel encoded by the nucleic acid sequence represented by SEQ ID NO:3. SEQ ID NO:3 is a human gene that is not present in any non-human species of animal.

Mullins teaches a transgenic rat that does not comprise the potassium transport channel encoded by the nucleic acid set forth by SEQ ID NO:3 and is therefore deficient in the expression of the potassium transport channel encoded by the nucleic acid sequence represented by SEQ ID NO:3.

Therefore, Mullins fulfills all of the limitations of claim 32.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is 703-305-5469. The examiner can normally be reached on Mon-Weds 6:00-2:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on 703-305-4051. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

Valarie Bertoglio
Examiner
Art Unit 1632

A handwritten signature in black ink, appearing to read 'Michael Wilson', with a stylized, flowing script.

MICHAEL WILSON
PRIMARY EXAMINER